IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Applicant:	ABBOTT, Nicholas L.
Application No.:	10/711,517
Filing Date:	September 23, 2004
Title:	USING LIQUID CRYSTALS TO DETECT AFFINITY MICROCONTACT PRINTED BIOMOLECULES
Atty Docket No.:	960296.00526
Examiner:	FOSTER, Christine E.
Group Art Unit:	1641

DECLARATION UNDER RULE 1.132

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

1. I, Nicholas L. Abbott, the undersigned declare as follows:

2. All statements made herein are true to the best of my knowledge, or if made upon information and belief are believed to be true.

3. I received a Ph.D. in Chemical Engineering from Massachusetts Institute of Technology and performed my post-Doctoral work at Harvard University in the Department of Chemistry. I have been a professor of Chemical and Biological Engineering at the University of Wisconsin-Madison since 1998. My areas of research interest include liquid crystal technology, interfacial phenomena, colloid chemistry, nano-scale science and polymers. I have over 200 peer reviewed publications in these fields.

4. I am the first-named inventor of the above captioned patent application. Accordingly, I am completely familiar with the subject matter of this patent application. I have reviewed the final Office Action dated December 4, 2007 as well as both Bernard et al. and Renault et al., the

two primary documents cited against the claims in the Office Action. Finally, I am the first named inventor of Abbott et al., which is cited against the claims as a secondary document. Accordingly, I am completely familiar with the subject matter of that patent as well. I am submitting this declaration to provide further evidence that the skilled artisan at the time of the invention considering Bernard/Renault in light of Abbott et al. could not have predictably used the teachings of the cited documents to practice our claimed method.

5. In developing the method of the present invention, we had to develop detection surfaces that would do two things. First, the detection surfaces used must be capable of capturing analyte when the stamp is brought into contact with the detection surface. The surfaces used in the current application have surface properties such that they capture analytes without specificity; specificity is achieved instead by placement of the receptor on the stamp. In contrast, a self-assembled monolayer formed from an alkanethiol, as described by Abbott et al., will not capture analytes from a stamp. Instead, the surfaces used in Abbott were subsequently functionalized with a receptor to specifically capture one analyte and not another.

6. Second, we had to develop surfaces that would not only capture the analyte from the stamp, but would also give rise to distinguishable orientations in liquid crystal anchoring depending on whether or not the analyte was on the surface. In order for a detectable change to occur in the orientation of the liquid crystal upon capture of the analyte, the detection surface has to be capable of uniformly anchoring liquid crystal in the absence of analyte. The present application teaches the skilled artisan to successfully create surfaces having these two properties; the combination of Bernard/Renault in light of Abbott et al. does not.

7. As to the detection surfaces taught by Bernard/Renault (glass and polystyrene), such surfaces when untreated or uncoated are not capable of uniformly anchoring liquid crystal. Although glass or polystyrene can be used as a supporting substrate for liquid crystal based detection surfaces, an additional anchoring layer must be deposited on the glass to enable liquid crystal-based detection on the surface. This is because uncoated glass or polystyrene surfaces generally do not uniformly anchor liquid crystal.

In support of this statement, we and others have collected experimental data showing that the orientation of liquid crystals are planar on both uncoated glass and polystyrene surfaces, the detection surfaces taught by Bernard/Renault. In particular, the following two references describe the planar anchoring of liquid crystals on glass ((a) Cognard, J., *Alignment of Nematic Liquid-Crystals and Their Mixtures.* Molecular Crystals and Liquid Crystals, 1982: p. 1-77. (b) Janning, J.L., *Thin-Film Surface Orientation for Liquid-Crystals.* Applied Physics Letters, 1972. **21**(4): p. 173-&.) and the following two references describe planar anchoring of liquid crystals on polystyrene. ((a) Kang, H., J.C. Lee, and D. Kang, *The Effect of Phenoxymethyl Side Groups on the Liquid Crystal Alignment Behavior of Polystyrene Derivatives.* Macromolecular Research, 2009. **17**(7): p. 506-515. (b) Hyo, K., K. Tae-Ho, K. Daeseung, and L. Jong-Chan, *4-Alkylphenoxymethyl-Substituted Polystyrenes for Liquid Crystal Alignment Layers.* Macromolecular Chemistry and Physics, 2009. **210**(11): p. 926-935.

8. In addition, our data show that the orientation of liquid crystals on protein (analyte)-coated glass or polystyrene surfaces are also planar; so the orientation of liquid crystals is the same on glass or polystyrene surfaces independent of whether or not protein (analyte) is on the surface. Thus, the presence of analyte on the surface can not be established by using liquid crystal-based detection on a bare glass or polystyrene detection surface.

9. The Office asserts that that one considering Bernard/Renault in light of Abbott et al. would have had a reasonable expectation of success in practicing the presently claimed method "because the detection surfaces taught by Renault et al. (glass and/or polystyrene) are taught by Abbott et al. as suitable substrates for liquid crystal detection (see Abbott et al. at columns 14-15)." Importantly, the cited section notes that additional surface components may be coated onto the substrate (see col. 15, lines 1-8) and that the anchoring of the liquid crystal depends on the nature of the substrate surface, not on the composition of the substrate support (see col. 16, lines 47-49). For example, liquid crystal anchoring can be established by the deposition of specialized organic surfaces (i.e. self-assembled monolayers, or SAMs) over a substrate surface such as metal (see col. 18 and the Examples). Thus, although Abbott et al. teach that glass could be used as a substrate support for a liquid-crystal based detection surface, they do not teach that untreated

glass with no additional detection surface coating could be successfully used as a detection surface for liquid crystal-based detection. Indeed, at the time of the invention, the skilled artisan would have understood that such a surface would not work successfully, because the liquid crystal would not be appropriately anchored on such a surface.

10. The Office also asserts that one would have a reasonable expectation of success in affinity stamping of the surface of Abbott et al. according to the method of Bernard/Renault, because the surface of Abbott et al. "is compatible with microcontact printing (see col. 17, lines 5-22)." The cited section describes the use of microcontact printing to print microfabricated detection surface patterns onto a base substrate material such as glass. The microprinted sections of the patterns then act as detection surfaces. If the substrate on which the pattern is printed is untreated glass, the unprinted areas of the surface could not themselves function as detection surfaces, as discussed above. There is no suggestion that microcontact printing would be compatible for use on the resulting microfabricated detection surfaces to deliver analyte to those detection surfaces (rather than to the bare glass), as claimed in the present invention.

11. In fact, we had to overcome a number of technical challenges to develop a detection surface that appropriately anchored liquid crystals while successfully non-specifically binding analytes delivered to the detection surface by affinity microcontact printing. The detection surfaces described in Abbott et al. were not intended to capture analyte delivered by affinity microcontact printing, and in fact, will not capture analyte using the claimed method. For example, we discovered that the self-assembled monolayers comprised of alkanethiols having the structure $CH_3(CH_2)_nSH$ (column 18 of Abbott et al.) do not work to detect molecular interactions using affinity microcontact printing to deliver the analyte. The liquid crystals simply do not report the presence of the targeted analytes. Furthermore, we found that other surfaces described in Abbott et al., including surfaces comprising the compound formula $CF_3(CF_2)_nZ(CH_2)_pSH$ (described in column 23), are also not suitable for use with the present method.

12. Our development of detection surfaces having the necessary properties for successful use with the presently claimed method was a long and difficult process, requiring a substantial

investment of time and money. Based on the teachings of the cited documents, our eventual success in developing such detection surfaces would not have been predicted or expected.

13. This declaration is made with knowledge that willful false statements and the like are punishable by fine or imprisonment, or both under 18 USC Sec. 1001, and may jeopardize the validity of the subject patent application or any patent issuing thereon.

Dated: MARCH 16, 2010

Nicholas L. Abbott

Nicholas L. Abbott, Ph.D.
Professor
Department of Chemical and Biological Engineering
University of Wisconsin-Madison
3016 Engineering Hall
1415 Engineering Drive
Madison, WI 53706